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# Association between extreme temperature and kidney disease in South Korea, 2003–2013: Stratified by sex and age groups

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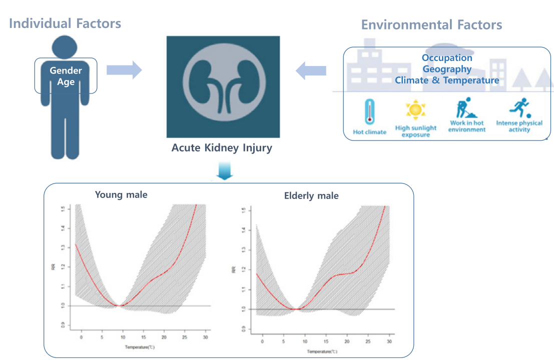
## HIGHLIGHTS

- We observed an association between high temperature and hospital admissions of kidney diseases in South Korea.
- The effect on acute kidney injury hospitalization was significant, but the effect on chronic kidney disease was not.
- We found interactions between gender and age in the association between kidney morbidity and high temperature.

## GRAPHICAL ABSTRACT

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## ABSTRACT

Weather conditions due to climate change affect the health directly and indirectly. Previous studies have shown associations with temperature, heat wave, and cold spell, and these do not only result in mortality from cardiovascular disease, respiratory disease, etc., but also in morbidity. This study aimed to quantify the relative risk for hospital admissions related to ambient temperature for genitourinary system diseases, which are representative of metabolic disease. We conducted a nationwide retrospective cohort study using claims data generated by medical services for diseases of the urinary system. The data was based on medical claims data from 16 districts in South Korea, to the nationwide level between 2003 and 2013. A total of 1,255,671 hospital admissions through the emergency department because of diseases of the genitourinary system were reported within the study period. The overall cumulative relative risk at the 99th percentile vs. the minimum morbidity percentile for renal diseases was 1.252 (95% confidence interval 1.211 to 1.294) in Seoul, 1.252 (1.21 to 1.296) in Busan, 1.236 (1.196 to 1.276) in Daegu, 1.237(1.197 to 1.279) in Gwangju, and 1.258 (1.218 to 1.299) in Gyeonggi-do, 1.278 (1.211 to 1.349) in Chungcheongbuk-do, 1.291 (1.235 to 1.35) in Gyeongsangnam-do. In the group of men over 65 years, the overall cumulative RR was high and statistically significant in acute kidney injury (AKI). But we could not find the effect of high temperature for chronic kidney disease (CKD). The association were rather opposite, but not statistically significant. Our nationwide study not only demonstrates relative risk considering lag effects associated with ambient temperature and trends in hospital admissions through the emergency department for genitourinary disorders but also observed differences among disease groups.



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## 1. Introduction

As temperature increases, patients with baseline diseases may face increased risk due to various disease pathways, with an associated increased use of medical services. Diabetes mellitus, hypertension, glomerulonephritis, renal vascular disease, and many other nephrotoxic factors cause progressive damage to kidney function, and the effect of heat stress speeds this progression to overt disease. This study focused on diseases occurring in organs of the urinary system, which are representative of metabolic disease. Exposure to high temperature and environmental heat is accompanied by perspiration and fluid loss (dehydration), followed by volume depletion and hypovolemia. These can cause hypotension, and could lead to shock, coma, and sudden death thereafter. Dehydration, volume depletion, and hypovolemia can also lead to the formation of kidney stones and, thus, renal colic. Hypovolemia can result in serum electrolyte imbalance, which can cause arrhythmias, coma, and sudden death, as well as acute renal failure (Harlan et al., 2014). Heat stress leads to volume depletion, and, if it becomes serious, volume depletion may cause acute kidney injury even in healthy individuals (Semenza et al., 1999; Kovats et al., 2004; Knowlton et al., 2009). In the absence of functional recovery from the initial injury, acute kidney injury leads to chronic kidney disease (CKD) (Chawla and Kimmel, 2012). Recent studies have shown that subclinical damage also increases the risk of kidney disease, in countries such as Central America, Sri Lanka and India, male labors in the rural area are concerned about an increase in CKD (Glaser et al., 2016). Hyperthermia-induced volume depletion is one of the subclinical injuries to the kidney that may progress to kidney disease (Levin et al., 2008; Venkatachalam et al., 2010).

Many previous studies have been conducted on heat waves and various heat-related illnesses (Knowlton et al., 2009; Green et al., 2010; Lin et al., 2013; Wang et al., 2013; Condemi et al., 2015), and have examined heat stress and related renal dysfunction (Patnala et al., 2014; Moyce et al., 2017). These studies were conducted only in a limited study area, which included only several regions or cities in the country. Moreover, most of these studies were conducted in Western countries. In Australia, based on studies on the relationship between heat threshold and temperature, renal health outcomes have been associated with temperature (Williams et al., 2012) similar to the findings for other regions (Green et al., 2010; Basu et al., 2012; Condemi et al., 2015).

Impact assessments of association between extreme temperature and mortality and morbidity were conducted, but the vulnerable groups varied and were still controversial depending health outcome, regions and type of diseases. Most studies suggest that the very old and the very young are most vulnerable on the effects of extreme heat (Kravchenko et al., 2013; Gronlund et al., 2016). Vulnerability may vary according to sex; during the California heat wave of 2006, the mortality rate among women was higher than among men. Heat-associated hospitalizations for renal diseases were significantly higher people aged 25–44 years in a New York study (Fletcher et al., 2012). In general, the association between temperature and morbidity was analyzed as a whole, male, female, younger and older group. Because these age and sex are a vulnerable determinant of the temperature rise due to climate change and can also be a risk factor for the pathogenesis of the disease.

This study was conducted to evaluate the effects of a specific disease to nationwide level and examined the effects of high temperature on the quantification and characteristics of sex by age.

In order to investigate the effects and patterns of high-temperature on kidney disease with medical utilization data from Korea National Health Insurance Service (NHIS) included patients diagnosed with diseases of the genitourinary system on a national scale.

## 2. Materials and methods

### 2.1. Study population and data sources

We obtained the health insurance claims data from the National Health Insurance Services between 2003 and 2013. The distribution and daily number of hospital admissions varied because access to medical services depended on the day of week or on scheduled admissions. Therefore, we included only hospital admissions through the emergency department. Diseases for these admissions were classified based on the International Classification of Diseases, 10th revision. The daily number of admissions with a principal discharge diagnosis of renal disease (N00–N39) was assessed. We included acute renal failure (N17), chronic kidney disease (N18) as being representative of acute and chronic disease etiologies (Nitschke et al., 2007; Fletcher et al., 2012; Vaneckova and Bambrick, 2013; Harlan et al., 2014; Wang et al., 2014). We included only hospital admissions cases through emergency visit in order to remove regular hospital admissions cases due to characteristics of chronic disease and then explored to effects of extreme temperature. Climate data for the study period were obtained from the Korea Meteorological Administration. Daily mean ambient air temperatures and relative humidity for the 16 districts were accessed from a monitoring station. Daily air pollution monitoring records were obtained from the National Institute of Environmental Research.

### 2.2. Statistical analysis

Analyses were performed using R software, in particular, packages dlnm and mvmeta. We accounted for the effects of ambient temperature by including the mean daily concentrations of $PM_{10}$ and the influence of relative humidity and day of the week on the effects of temperature and use of medical services. The distributed lag non-linear model (dlnm) assumes that the bi-dimensional exposure-lag-response association between ambient temperature and morbidity were estimated in each district. We used distributed lag non-linear models (DLNMs) to quantify the excess risk associated with ambient temperature on hospital admissions through the emergency department based on the National Health Insurance inpatient billing records. The association between daily average temperature and daily cause-specific hospital admissions was evaluated using DLNM with quasi-Poisson distribution. Natural cubic spline DLNM models were used to analyze the non-linear and delayed effects of temperature. The cross-basis function contained the dimensions of variables and lag days; we estimated the cumulative relative risk (RR) of ambient temperature lag for 7 days. For this study, we equally spaced knots of variables at spaced quantiles of the predictor and the knots of lag at equally spaced values on the log scale of lags. RR due to temperature was estimated using the cross-basis function in DLNM models. To estimate the effect of ambient temperature, the cumulative RRs and 95% confidence intervals of each cause-specific case were estimated by comparing the risk associated with the extreme temperatures of the 90th and 99th percentiles with that at the temperature associated with the lowest cause-specific disease (the centered temperature) (Gasparrini et al., 2010):

$$\log[\mathrm{E}(Y_t)] = \alpha + CB(mean\ temperature : lag7) + ns(Time, 4 \times year) + covariates$$

where $[\mathrm{E}(Y_t)]$ is the expected number of daily hospital admissions through the emergency department. Covariates were the day of the week, mean $PM_{10}$, and relative humidity. Fitted multivariate meta-regression models were used to derive the best linear unbiased district from the overall cumulative exposure-response association of each district. The best linear unbiased district represents a trade-off between the district-specific association provided by the first-stage regression and the pooled association. District-pooled lag–response relationships at the 99th temperature percentile were also derived from the re-centered

estimates using location-specific MMTs derived from best linear unbiased predictions (BLUPs). Meta-regression models allowed district-specific exposure–response and lag–response relationships. The fitted multivariate meta-regression models were then used to derive the BLUP of the overall cumulative exposure–response associations in each district (Gasparrini et al., 2012).

## 3. Results

### 3.1. Study population characteristics

There were 1,255,672 (total population: 47,990,761; census data in 2010) emergency hospitalized patients due to diseases of the genitourinary system in South Korea from 2003 to 2013. We classify patients according to patient identification numbers among patients who have been diagnosed with kidney disease and have used medical care once every year. Table 1 summarizes the number of cases admitted through the emergency department by age group and sex.

In the acute renal disease group, for all age groups except age ≥65 group, the number of male patients was higher than the number of female patients, but in the renal disease group, the number of female patients was higher than the number of male patients in all age groups except the 0–4 and 10–14 age group (Table 1). Table S1 showed the distribution of hospitalized cases through the emergency departments in the 16 administrative districts. The highest number of daily medical services use was reported in Gyeonggi-do, Seoul, and Gyeongsang buk-do. Average values were observed to be higher in Gyeonggi Province, Seoul, and Busan, in that order.

### 3.2. Meteorological data and extreme temperature effects

For each of the 16 districts, the distributions for all seasons, summer, and winter are shown for one year, with the daily mean temperature (Table S2 in the Supplement). The highest daily average temperature during the entire study period was 33.10 °C, which was recorded in Ulsan. Daegu followed with a temperature of 32.9°Cand Seoul with 31.8 °C. Fig. 1 showed the overall cumulative exposure-response curves (best linear unbiased predictions) for the 16 districts with the corresponding minimum morbidity temperature (MMT), i.e., the temperature with the minimum relative risk (RR) and the cut-offs to define extreme temperatures. The temperature distribution emphasizes how the hot temperature range, characterized by a high RR, comprises only a small proportion of the day. The overall cumulative RR at the 99th percentile vs the minimum morbidity temperature was significant throughout the 16 districts and was greater than the RR of the 90th percentile vs the minimum morbidity temperature (Table 2). The districts showed different optimal summer temperatures, represented by MMTs ranging from the 1 °C in Gyeonggi-do to 14 °C in the Jeju, as displayed in Table 2. These relationships suggest an excess morbidity risk associated with high temperatures in all the districts, with the strongest estimated effects in Gyeongsangnam-do and Jeollabuk-do summarized by an RR at the 99th percentile versus the MMT of 1.261 (1.198 to 1.328) and 1.243 (1.185 to 1.303), respectively. The lowest risk for the 99th percentile was estimated in Jeju-do, with an RR of 1.202 (1.141 to 1.266). In acute renal failure (N17), the overall cumulative RR at 99th percentile versus minimum morbidity temperature was statistically significant in all districts except Gangwondo, Chungcheongnamdo, Jeollabukdo and Gyeongsangbuk-do. Regarding specific diseases, renal disease (N00-N39) RR values were significant across the 16 regions.

Fig. 2 shows the districts-pooled lag-response relationships at the 99th temperature percentile by disease groups, which represent all genitourinary system (N00-N99) including acute renal failure (N17) and renal disease (N00-N39). The range of the temperature at which the RR of overall cumulative exposure-response associations on diseases of the genitourinary system was from 8 °C to 15 °C. However, there was no effect at high temperature on chronic kidney disease (Fig. 2).

### 3.3. The effects of stratified by sex and age groups

When we investigated the overall cumulative RR by group, in the disease group (N00-N99), all patients, the women, men and under 65 age groups showed statistical significance in all regions at the 90th percentile vs the MMT. The elderly group showed statistical significance in all regions except Jeollanam-do. The RR of the 90th percentile vs the MMT of the young (age < 65) and women groups was the high in these five groups (all patients, male, female, age <65 and age ≥65 group). In particular, the overall cumulative RR for women in the Jeollanam-do region was the highest. In the 99th percentile compared to MMT, the overall cumulative RR increased in the female group in the Seoul, Daejeon and Jeju-do regions. In the seven major cities (i.e Seoul, Busan, Daegu,Incheon, Gwangju, Daejeon and Ulsan), Gyeonggi-do, and Gyeongsangnam-do, the RR in the elderly population group was significant and in the other regions, female and age <65 years old group were overall cumulative RR at the 99th percentile, as compared to MMT (Fig. 3). By disease groups, in renal disease (N00-N39), the trends of the overall cumulative RR was similar to that in diseases of

**Table 1**
Number of the hospital admissions through emergency department visits by age group and sex.

| Disease | Acute renal failure (N17) | | Chronic kidney disease (N18) | | Unspecified renal failure (N19) | | Renal disease (N00-N39) | | Disease of the genitourinary system (N00-N99) | |
|---|---|---|---|---|---|---|---|---|---|---|
| Age group | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female |
| 0–4 | 185 | 144 | 95 | 29 | 15 | 7 | 42,329 | 29,540 | 44,955 | 29,711 |
| 5–9 | 82 | 69 | 128 | 54 | 7 | 4 | 5429 | 6856 | 7421 | 7105 |
| 10–14 | 170 | 117 | 203 | 133 | 10 | 3 | 3697 | 3594 | 6107 | 5565 |
| 15–19 | 449 | 201 | 361 | 272 | 21 | 13 | 4361 | 7425 | 6465 | 15,758 |
| 20–24 | 541 | 296 | 615 | 464 | 24 | 8 | 5803 | 17,143 | 7000 | 38,321 |
| 25–29 | 889 | 457 | 1298 | 1191 | 38 | 34 | 10,376 | 22,434 | 11,415 | 53,932 |
| 30–34 | 1202 | 566 | 2367 | 2150 | 53 | 27 | 14,303 | 23,475 | 15,594 | 57,770 |
| 35–39 | 1443 | 661 | 3356 | 2791 | 67 | 38 | 17,358 | 24,017 | 18,889 | 50,499 |
| 40–44 | 2021 | 766 | 5024 | 3708 | 103 | 53 | 20,440 | 28,254 | 22,578 | 51,662 |
| 45–49 | 2705 | 988 | 7734 | 5683 | 140 | 77 | 25,268 | 35,519 | 28,200 | 56,488 |
| 50–54 | 3277 | 1344 | 11,146 | 8098 | 179 | 96 | 29,501 | 39,682 | 33,906 | 50,560 |
| 55–59 | 3479 | 1502 | 13,142 | 9573 | 186 | 115 | 30,332 | 37,395 | 36,041 | 41,310 |
| 60–64 | 3768 | 1928 | 14,829 | 11,378 | 210 | 149 | 31,993 | 37,664 | 39,366 | 40,340 |
| 65–69 | 4728 | 3231 | 16,824 | 13,748 | 262 | 191 | 35,889 | 45,130 | 45,748 | 47,598 |
| 70–74 | 5848 | 4976 | 16,132 | 14,059 | 329 | 274 | 37,159 | 52,602 | 48,377 | 54,659 |
| 75–79 | 5459 | 5895 | 11,608 | 11,556 | 329 | 330 | 29,903 | 50,124 | 39,805 | 51,493 |
| 80+ | 7088 | 9856 | 10,119 | 11,058 | 445 | 611 | 32,523 | 64,527 | 42,860 | 66,194 |

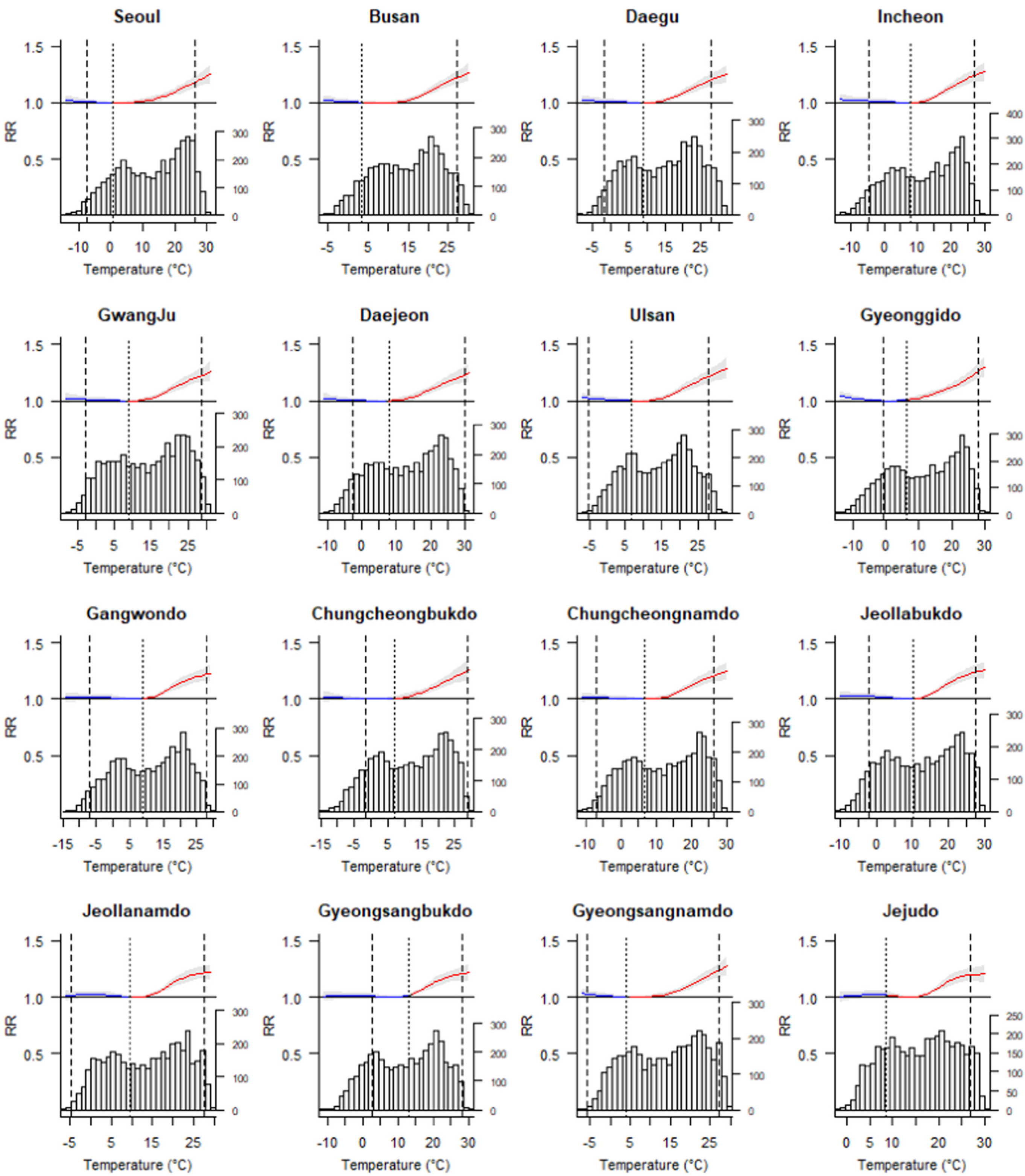


**Fig. 1.** Overall cumulative exposure-response associations on disease of the genitourinary system (N00-N99) in 16 districts.

the genitourinary system (N00-N99) however, size of the overall cumulative RR was higher than those of diseases of the genitourinary system (N00-N99) (Fig. 4). Second, in acute renal disease, the overall cumulative RR of the male was high in all regions at both the 90th percentile and the 99th percentile compared to MMT (Fig. 5). It showed a completely different from the result of the all genitourinary system (N00-N99).

We examined the effects of sex by type of kidney disease on the associations between renal disease type and temperature in the two age groups. In case of AKI disease, overall cumulative relative risk by region was higher than that of female in age <65 group and in age ≥ 65 groups, it of male was statistical significant but not female was significant (Table 3). When examining the effect of CKD by 4 groups (total, male, female, age <65 and age ≥65 groups).

**Table 2**
Overall cumulative relative risk of 90th percentile, 99th percentile versus minimum morbidity temperature (MMT) on diseases of the genitourinary system (N00-N99), acute renal failure (N17) and renal disease (N00-N39) hospital admissions through ER visits.

| Region | 90th vs MMT | | | 99th vs MMT | | | MMT |
|---|---|---|---|---|---|---|---|
| | RR | 95%CI | | RR | 95%CI | | |
| Diseases of the genitourinary system (N00-N99) | | | | | | | |
| Seoul | **1.155** | **1.114** | **1.197** | **1.204** | **1.155** | **1.255** | 2 |
| Busan | **1.166** | **1.125** | **1.209** | **1.223** | **1.172** | **1.277** | 9 |
| Daegu | **1.169** | **1.124** | **1.216** | **1.21** | **1.158** | **1.265** | 9 |
| Incheon | **1.195** | **1.147** | **1.245** | **1.239** | **1.183** | **1.297** | 7 |
| Gwangju | **1.168** | **1.122** | **1.215** | **1.209** | **1.156** | **1.265** | 9 |
| Daejeon | **1.171** | **1.123** | **1.221** | **1.212** | **1.156** | **1.271** | 6 |
| Ulsan | **1.16** | **1.113** | **1.209** | **1.213** | **1.163** | **1.265** | 9 |
| Gyeonggido | **1.169** | **1.129** | **1.21** | **1.226** | **1.178** | **1.276** | 1 |
| Gangwondo | **1.182** | **1.134** | **1.232** | **1.212** | **1.147** | **1.281** | 7 |
| Chungcheongbukdo | **1.189** | **1.137** | **1.243** | **1.234** | **1.162** | **1.31** | 2 |
| Chungcheongnamdo | **1.185** | **1.138** | **1.235** | **1.218** | **1.162** | **1.278** | 7 |
| Jeollabukdo | **1.218** | **1.17** | **1.268** | **1.243** | **1.185** | **1.303** | 9 |
| Jeollanamdo | **1.206** | **1.155** | **1.259** | **1.221** | **1.156** | **1.289** | 11 |
| Gyeongsangbukdo | **1.179** | **1.131** | **1.23** | **1.205** | **1.147** | **1.265** | 9 |
| Gyeongsangnamdo | **1.206** | **1.158** | **1.257** | **1.261** | **1.198** | **1.328** | 7 |
| Jejudo | **1.194** | **1.142** | **1.247** | **1.202** | **1.141** | **1.266** | 14 |
| Acute renal failure (N17) | | | | | | | |
| Seoul | **1.124** | **1.03** | **1.227** | **1.239** | **1.085** | **1.415** | 2 |
| Busan | **1.127** | **1.038** | **1.224** | **1.297** | **1.114** | **1.51** | 7 |
| Daegu | **1.111** | **1.016** | **1.215** | **1.235** | **1.041** | **1.465** | 5 |
| Incheon | **1.117** | **1.018** | **1.224** | **1.234** | **1.043** | **1.46** | 2 |
| Gwangju | **1.106** | **1.006** | **1.216** | **1.21** | **1.007** | **1.455** | 5 |
| Daejeon | **1.115** | **1.009** | **1.232** | **1.197** | **1.007** | **1.423** | 3 |
| Ulsan | **1.091** | **1.007** | **1.181** | **1.223** | **1.034** | **1.448** | 6 |
| Gyeonggido | **1.158** | **1.062** | **1.264** | **1.3** | **1.144** | **1.477** | 1 |
| Gangwondo | 1.086 | 0.97 | 1.216 | 1.086 | 0.895 | 1.319 | 1 |
| Chungcheongbukdo | **1.211** | **1.063** | **1.379** | **1.347** | **1.1** | **1.65** | 1 |
| Chungcheongnamdo | **1.106** | **1.001** | **1.222** | 1.164 | 0.99 | 1.369 | 3 |
| Jeollabukdo | 1.087 | 0.98 | 1.205 | 1.111 | 0.947 | 1.304 | 3 |
| Jeollanamdo | **1.194** | **1.065** | **1.339** | **1.328** | **1.115** | **1.582** | 5 |
| Gyeongsangbukdo | 1.082 | 0.984 | 1.191 | 1.119 | 0.951 | 1.316 | 3 |
| Gyeongsangnamdo | **1.176** | **1.052** | **1.314** | **1.292** | **1.092** | **1.529** | 5 |
| Jejudo | **1.225** | **1.083** | **1.386** | **1.428** | **1.155** | **1.766** | 9 |
| Renal disease (N00-N39) | | | | | | | |
| Seoul | **1.181** | **1.143** | **1.221** | **1.252** | **1.211** | **1.294** | 4 |
| Busan | **1.184** | **1.147** | **1.221** | **1.252** | **1.21** | **1.296** | 9 |
| Daegu | **1.185** | **1.145** | **1.225** | **1.236** | **1.196** | **1.276** | 10 |
| Incheon | **1.193** | **1.149** | **1.238** | **1.253** | **1.212** | **1.296** | 6 |
| Gwangju | **1.183** | **1.144** | **1.223** | **1.237** | **1.197** | **1.279** | 9 |
| Daejeon | **1.193** | **1.15** | **1.237** | **1.247** | **1.204** | **1.292** | 6 |
| Ulsan | **1.154** | **1.106** | **1.203** | **1.227** | **1.192** | **1.263** | 7 |
| Gyeonggido | **1.189** | **1.153** | **1.225** | **1.258** | **1.218** | **1.299** | 3 |
| Gangwondo | **1.21** | **1.17** | **1.252** | **1.228** | **1.17** | **1.288** | −14 |
| Chungcheongbukdo | **1.219** | **1.177** | **1.263** | **1.278** | **1.211** | **1.349** | 4 |
| Chungcheongnamdo | **1.208** | **1.168** | **1.249** | **1.246** | **1.202** | **1.292** | 7 |
| Jeollabukdo | **1.228** | **1.189** | **1.268** | **1.251** | **1.206** | **1.299** | 9 |
| Jeollanamdo | **1.227** | **1.188** | **1.268** | **1.227** | **1.173** | **1.283** | −6 |
| Gyeongsangbukdo | **1.21** | **1.169** | **1.253** | **1.242** | **1.197** | **1.288** | 9 |
| Gyeongsangnamdo | **1.221** | **1.182** | **1.261** | **1.291** | **1.235** | **1.35** | 7 |
| Jejudo | **1.232** | **1.191** | **1.274** | **1.227** | **1.176** | **1.279** | −1.5 |

p-value < 0.05

## 4. Discussion

We found an association between heat exposure and increased hospital admissions for genitourinary system diseases in South Korea. Our analysis of 16 Korean districts yielded several notable findings. Most importantly, we observed differences among disease groups. Our results are consistent with the current understanding of the pathophysiological processes associated with exposure to heat. The effects of high temperature on metabolic diseases, diabetes, and genitourinary morbidity increased with heat and longer lag periods (Kenny et al., 2010). The burden of renal morbidity may increase in susceptible individuals as an indirect consequence of global warming (Hansen et al., 2008). During heat exposure, the diversion of blood from the splanchnic and renal vasculature to the periphery can stress the renal system. There is evidence that exposure to heat causes dehydration and hyperthermia and results in renal dysfunction. In hyperthermia, the thermoregulatory physiological and circulatory mechanisms are necessary to overcome extreme heat conditions. These may cause mild to moderate renal hypoperfusion following hypohydration and peripheral vasodilation, leading to stress on the kidneys. Acute kidney injury is one of the complications of heat stress (Vertel and Knochel, 1967). Recurrent heat exposure and dehydration, especially when accompanied with overexertion, can lead to several pathophysiologic processes including low grade or overt rhabdomyolysis, hyperosmolarity, hyperthermia, and extracellular volume depletion (Glaser et al., 2016).

These processes can result in several mechanisms that can lead to acute kidney injury (AKI), including the adverse effects of vasopressin (Bankir et al., 2013) and the fructokinase system (Jimenez et al., 2014) on renal tubules. The development of hyperuricemia and hyperuricosuria results in urate crystal formation (Roncal-Jimenez et al., 2016), hypokalemia-induced renal vasoconstriction, hypoxia and injury (Suga et al., 2001), and decreased renal blood flow that may also cause ischemic damage.

In our study, an effect of ambient apparent temperature on hospitalization for renal disease was consistent with previous studies conducted during heat waves. A study comprised of Chicago hospitalization data during the summer of 1995 revealed that a primary diagnosis of acute kidney injury was significantly elevated over baseline during the heat wave (Semenza et al., 1999). A study conducted in Adelaide in South Australia in summer, found that hospital admissions for acute kidney injury were increased during heat waves compared with non-heat waves, with an incidence rate ratio of 1.255 (1.037 to 1.519) (Hansen et al., 2008). A study conducted in California also found an increase in both emergency department visits and hospitalizations for acute renal failure during the heat wave period in 2006 (Knowlton et al., 2009). A study in New York revealed an overall 9% increase in the odds of hospitalization for acute renal failure per 2.78 °C increase in mean temperature with a 1 day lag (OR, 1.09; 95% CI, 1.07–1.12) (Fletcher et al., 2012).

There were 1565 emergency hospital admissions (EHAs) for renal diseases in children during the study period (1996–2005) in Brisbane, Australia. Heat waves exhibited a significant effect on EHAs for renal diseases in children after adjusting for confounding factors (OR, 3.6; 95% CI, 1.4 to 9.5) (Wang et al., 2014). These associations are biologically plausible because heat exposure causes blood to be redistributed away from splanchnic and renal vascular beds, putting additional stress on the renal system (Semenza et al., 1999).

Our finding was consistent with previous studies in which it was significant on the association between increased temperature and morbidity of renal disease (N00-N39) (Green et al., 2010; Kjellstrom et al., 2010; Lin et al., 2013). In renal disease (N00-N39) group, female who are known to be vulnerable to climate change were higher RR values than those of men. Studies have consistently demonstrated increasing renal related symptoms and injuries in the elderly during heat wave events (Nitschke et al., 2011; Wang et al., 2012). A recent study showed that the very elderly (85 + years) were the highest risk age group of renal diseases hospital admissions in Australia during heat waves (Hansen et al., 2008). However, this study showed that it increased RR in age group below 65 with renal disease than those of elderly groups known more vulnerable to the development of heat-related symptoms or illness, when analyzing age -stratified with two age groups (Figs. 4–5). To examine these results, we conducted the types of detailed diseases included in a large range of renal diseases (N00-N39). As a results, our data showed that the pattern of morbidity in relation to high temperature in acute kidney injury was different from the results of previous studies that increased the risk of AKI in elderly people in certain climatic zones (McTavish et al., 2017). In each group, male and the age group (age ≤ 64 years), the overall cumulative RR was high and statistically significant under acute kidney injury except 4 regions at an extreme temperature (99th percentile of mean temperature). Also, the overall cumulative RR of male showed a higher at an extreme

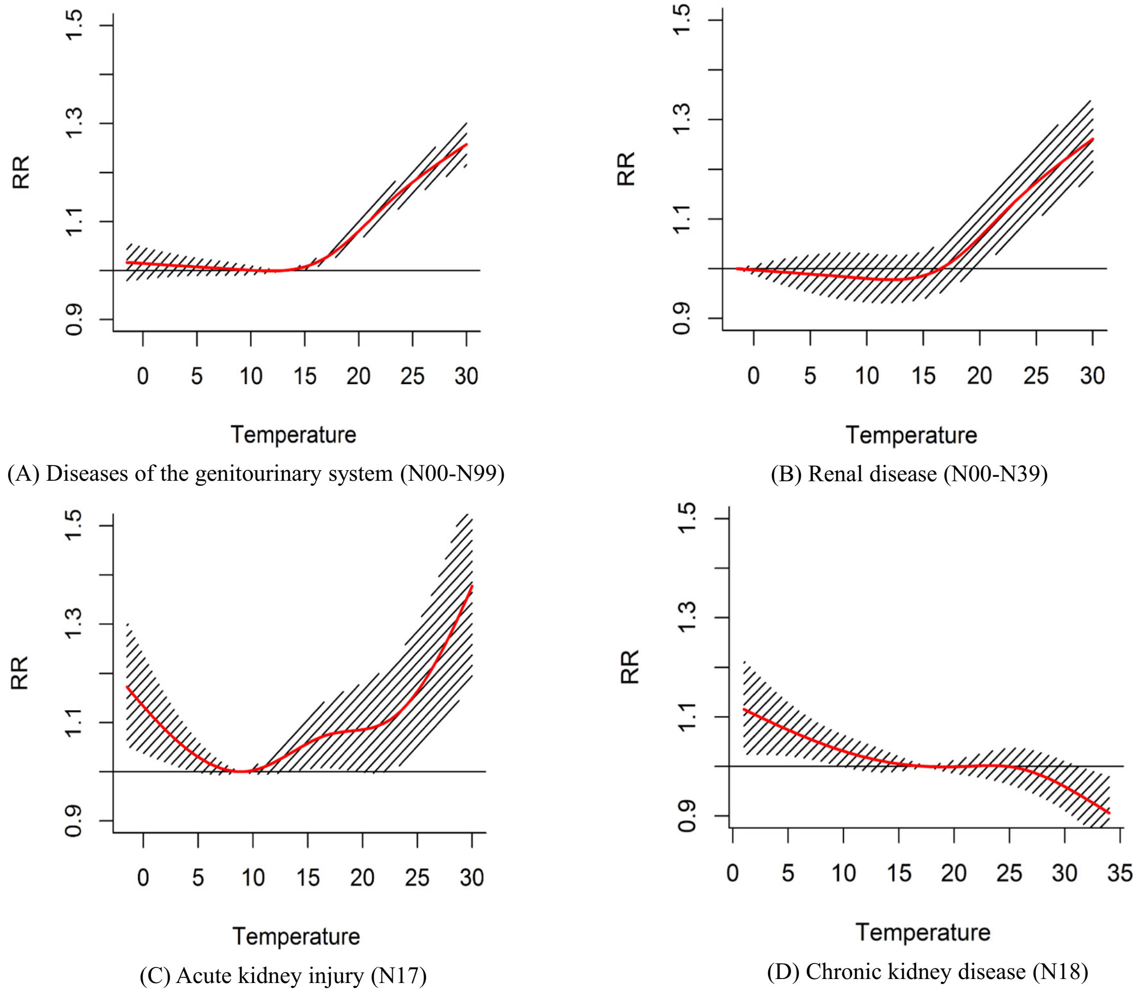


**Fig. 2.** Pooled overall cumulative temperature-morbidity association of the genitourinary system in 16 districts of South Korea, 2003–2013.

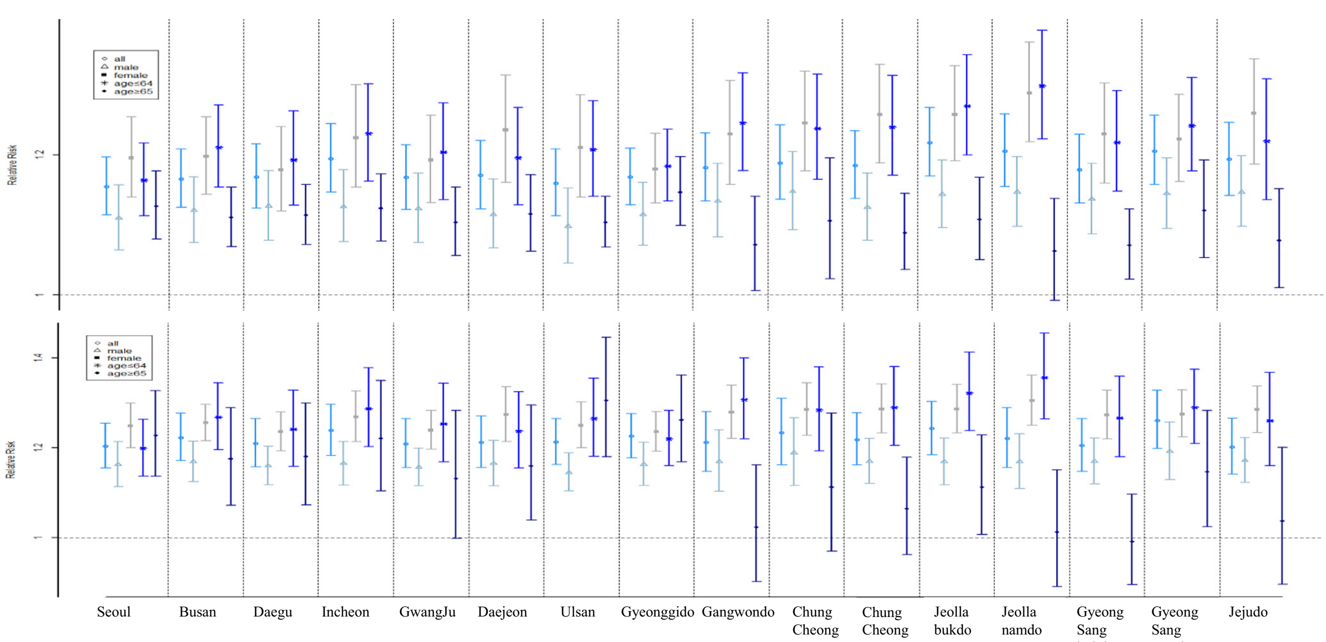


**Fig. 3.** Overall cumulative exposure-response associations of groups (all, male, female, age <65, age ≥65) at 90th percentile (top), 99th percentile (bottom) versus minimum morbidity temperature on diseases of the genitourinary system (N00-N99) hospital admissions through ER visits by districts.

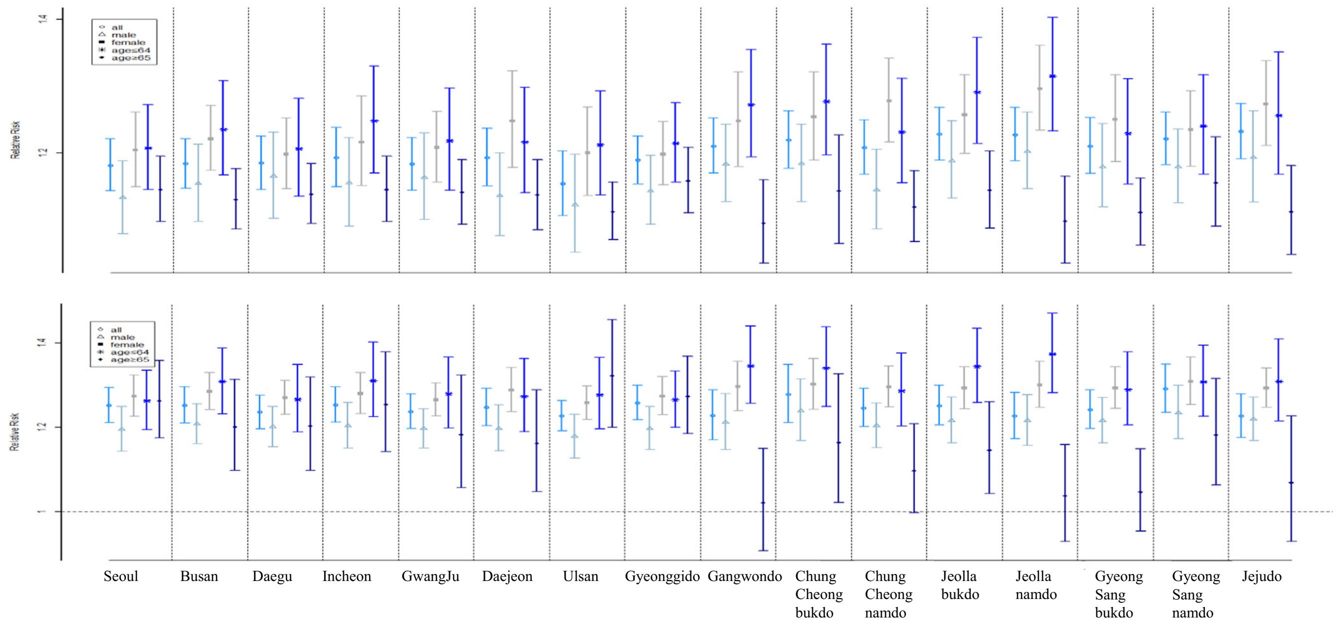


**Fig. 4.** Overall cumulative exposure-response associations of groups (all, male, female, age <65, age ≥65) at 90th percentile (top), 99th percentile (bottom) versus minimum morbidity temperature on acute renal disease (N00-N39) hospital admissions through ER visits by districts.

temperature (99th percentile of mean temperature) than those of female (Fig. 5). However, in the analysis of stratified by gender and age groups, these results were significant in the group of men over 65 years, whereas in the female, it did not show statistically significant results in two age groups in any regions (Table 3). The results may be considered as the increase of exposure to high temperature in men than that in women.

In previous studies in Adelaide, under AKI, IRR was statistically significantly higher in female among age < 65 years group than that of male and was similar in age ≥ 65 years groups but not statistically significant.

Recent studies have shown an increase in CKD morbidity in the hottest Pacific lowlands and in among sugarcane workers (Moyce et al., 2017; Nerbass et al., 2017). The risk of CKD in young men in rural areas is expected to increase. This is likely to increase the risk of CKD when exposed to long-term heatwaves due to repeated exposure to heat waves. In Adelaide, Australia study, incidence rate ratios of CKD was not significant, both emergency department and inpatient admissions.

This study has several strengths. First, very few studies of ambient temperature and morbidity have been conducted using data from several major cities, and this is the first study to focus on 16 districts of

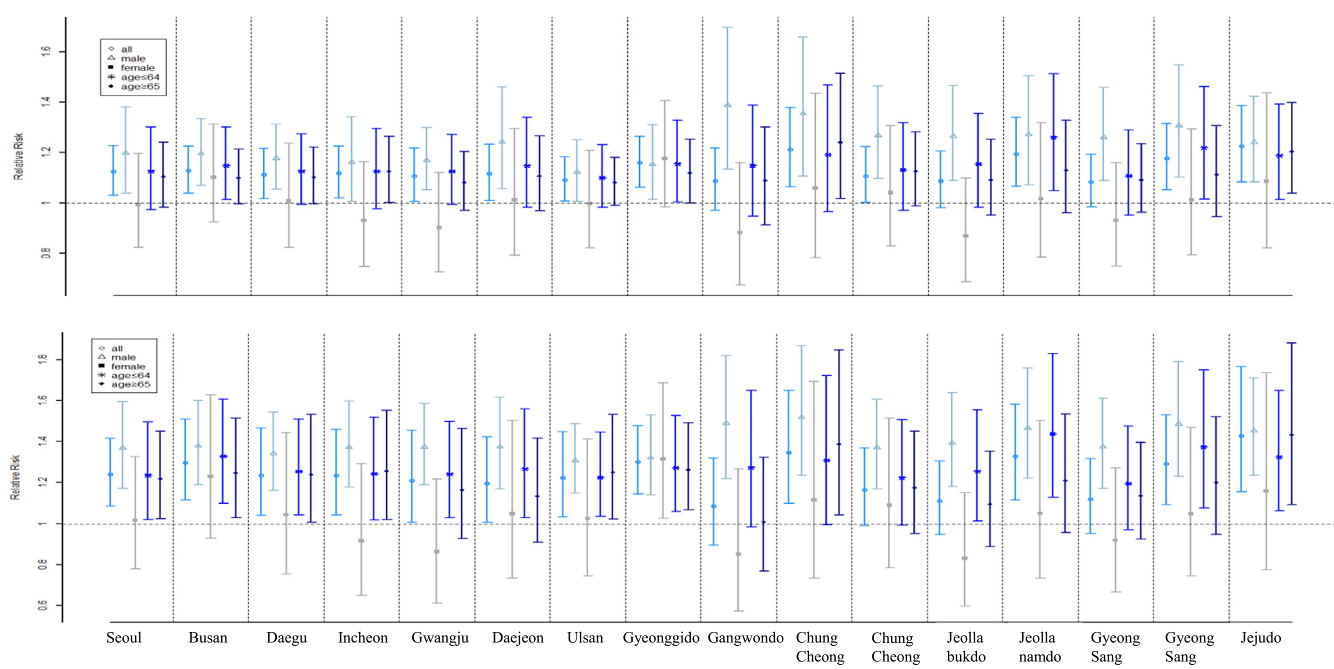


**Fig. 5.** Overall cumulative exposure-response associations of groups (all, male, female, age <65, age ≥65) at 90th percentile (top), 99th percentile (bottom) versus minimum morbidity temperature on acute kidney injury (N17) hospital admissions through ER visits by districts.

**Table 3**
Overall cumulative relative risk of 99th percentile versus minimum morbidity temperature (MMT) on acute kidney injury (N17) hospital admissions through ER visits.

| | | AKI | | | | | |
|---|---|---|---|---|---|---|---|
| | | Age ≤ 64 | | | Age ≥ 65 | | |
| Regions | Gender | RR | 95% CI | MMT | RR | 95% CI | MMT |
| Seoul | Female | 0.794 | 0.444–1.42 | 31 | 1.114 | 0.903–1.374 | 3 |
| | Male | **1.654** | **1.162–2.355** | 2 | **1.28** | **1.084–1.512** | 2 |
| Busan | Female | 0.986 | 0.54–1.801 | 22 | 1.194 | 0.946–1.508 | 7 |
| | Male | **1.561** | **1.113–2.188** | 6 | **1.308** | **1.12–1.527** | 5 |
| Daegu | Female | 0.857 | 0.443–1.658 | 25 | 1.113 | 0.874–1.419 | 6 |
| | Male | 1.405 | 0.993–1.989 | 6 | **1.276** | **1.104–1.475** | 3 |
| Incheon | Female | 0.698 | 0.324–1.5 | 27 | 1.024 | 0.806–1.301 | 4 |
| | Male | 1.229 | 0.817–1.849 | 4 | **1.294** | **1.103–1.52** | 1 |
| GwangJu | Female | 0.742 | 0.369–1.491 | 29 | 1.014 | 0.789–1.303 | 7 |
| | Male | **1.494** | **1.052–2.122** | 5 | **1.297** | **1.121–1.499** | 6 |
| Daejeon | Female | 0.732 | 0.323–1.66 | 24 | 1.063 | 0.834–1.354 | 4 |
| | Male | 1.376 | 0.889–2.132 | 4 | **1.339** | **1.122–1.597** | −1 |
| Ulsan | Female | 0.851 | 0.427–1.697 | 27 | 1.105 | 0.885–1.381 | 6 |
| | Male | 1.287 | 0.917–1.807 | 6 | **1.241** | **1.086–1.417** | 5 |
| Gyeonggido | Female | 1.603 | 0.934–2.751 | −14 | 1.192 | 0.971–1.464 | 2 |
| | Male | 1.172 | 0.847–1.622 | 18 | **1.278** | **1.092–1.496** | 18 |
| Gangwondo | Female | 0.588 | 0.237–1.459 | 23 | 0.989 | 0.746–1.311 | 29 |
| | Male | 1.577 | 0.933–2.665 | 1 | **1.486** | **1.18–1.871** | −4 |
| Chungcheongbukdo | Female | 0.559 | 0.219–1.425 | 24 | 1.174 | 0.87–1.583 | 2 |
| | Male | 1.674 | 0.973–2.878 | 1 | **1.484** | **1.168–1.885** | −2 |
| Chungcheongnamdo | Female | 0.975 | 0.461–2.061 | 21 | 1.053 | 0.826–1.341 | 4 |
| | Male | 1.294 | 0.863–1.94 | 4 | **1.35** | **1.142–1.595** | −2 |
| Jeollabukdo | Female | 0.794 | 0.375–1.681 | 30 | 0.976 | 0.764–1.247 | 30 |
| | Male | 1.491 | 0.983–2.261 | 3 | **1.353** | **1.137–1.609** | 0 |
| Jeollanamdo | Female | 1.095 | 0.464–2.583 | −6 | 1.091 | 0.838–1.421 | 6 |
| | Male | **1.819** | **1.132–2.922** | 4 | **1.366** | **1.121–1.665** | 5 |
| Gyeongsangbukdo | Female | 0.541 | 0.256–1.141 | 30 | 1.077 | 0.846–1.371 | 4 |
| | Male | 1.455 | 0.963–2.2 | 4 | **1.328** | **1.122–1.571** | 0 |
| Gyeongsangnamdo | Female | 1.187 | 0.535–2.632 | −7 | 1.139 | 0.873–1.485 | 6 |
| | Male | 1.499 | 0.952–2.358 | 5 | **1.385** | **1.13–1.696** | 4 |
| Jejudo | Female | 0.813 | 0.343–1.925 | 24.5 | 1.171 | 0.881–1.555 | 9.5 |
| | Male | **1.609** | **1.043–2.481** | 8.5 | **1.346** | **1.141–1.587** | 9.5 |

$p$-value < 0.05

South Korea. We were able to control the confounding factor of air pollution in our analysis to accurately determine positive associations between temperature and morbidity. There were also limitations to this study. Use of claims data limits the amount of individual-level data. We did not know where people spent most of their time, and work and leisure patterns affect actual exposure to high temperatures.

There may be variations among hospitals and physicians in terms of hospital admission criteria, assignment of diseases to primary and secondary diagnoses, and classification of diseases. In this study, we classified the diseases as acute renal failure (N17), renal disease (N00-N39), and genitourinary system diseases (N00-N99). The disease groups (N40-N99), except renal disease (N00-N39) and genitourinary system diseases (N00-N99), included breast and pelvic organ diseases that deviate from the category of urinary tract disease. However, the number of patients in the disease groups (N40-N99), except for renal disease (N00-N39), was not high. In relation to the rise in temperature, the increase in severity of renal disease groups (N00-N39) was significant.

## 5. Conclusion

At the extremes in apparent temperature, we observed an association between temperature and hospital admissions in South Korea. Reducing heat exposure and mitigating the effects of heat through adequate hydration during hot weather are important steps in reducing heat related morbidity. This study found that the vulnerable group to the effect of the kidney disease on the extreme temperature, depending on the disease type differs from the group defined as vulnerable to climate change in general. In other words, the results of the group that considered both gender and age showed different from results of the group that considers only sex or age. Therefore, when considering the effects of morbidity and extreme temperature, the characteristics of the disease should be considered.


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## Disclosure

All the authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

## Contributors

Ejin Kim designed data collection tools, monitored data collection for this study, wrote the statistical analysis plan, cleaned and analyzed the data, and drafted and revised the paper. She is guarantor. Yong Chul Kim and Jung Pyo Lee writed and revised the paper. Ho Kim initiated the collaborative project, designed data collection tools, monitored data collection for the study.

## Ethical approval

Ethical approval was obtained from research ethics committees (IRB No. E1707/002-002). Because the procedure being tested was not invasive or different from current clinical practice, and because outcome

data were routinely collected at NHIS and anonymously transmitted, no individual consent was sought.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2018.06.055.

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